REMARKS

Please reconsider the application in view of the following remarks. Applicant thanks the Examiner for carefully considering this application.

Disposition of Claims

Claims 1-20 are pending in this application. Claims 1 and 14 are independent. The remaining claims depend, directly or indirectly, from claim 1 or claim 14.

Rejection(s) under 35 U.S.C. § 103

Claims 1-20

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koketsu, et al. (J. Carbohydrate Chemistry, 1995, Vol. 14, No., p.833-841) (hereinafter "Koketsu 1995") and SCORE search result, in view of Yamamoto et al. (JP 08099988 A, 1996, abstract) (hereinafter "Yamamoto 1996") and further in view of Inazu, et al. (Peptide Science 1998, M. Kondo Edition, p.153-156) (hereinafter "Inazu") and Koketsu, et al. (The Journal of Food Science, 1993, Vol. 58, No. 4, pp. 743-747) (hereinafter "Koketsu 1993") and Yamamoto, K. (Journal of Bioscience and Bioengineering, 2001, Vol. 92, No. 6, pp. 493-501) (hereinafter "Yamamoto 2001"). This rejection is respectfully traversed.

"Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so. *In re Kahn*, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006) M.P.E.P. § 2143.01(I). (Emphasis added), *see also*, M.P.E.P. § 2143.01(VI).

Furthermore, MPEP § 2142 states that "impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." The fact that the Examiner relies on 5 references, none of which provides teaching or suggestion of a combination as asserted by the Examiner, to reject the present claims would suggest that the Examiner has committed impermissible hindsight reconstruction using applicant's application as a road map. Accordingly, this rejection should be withdrawn.

The present invention relates to methods for preparing asparagine-linked oligosaccharide derivatives by subjecting delipidated egg yolk to a two-step enzymatic process, i.e., first with a protease (proteinase) and then with a peptidase. The asparagine-linked oligosaccharides thus obtained are then derivatized with a lipophilic protecting group and then purified on a reverse-phase column.

Using this process, the asparagine-linked oligosaccharide derivatives, which contain only asparagine as amino acids, can be easily and efficiently produced. The resulting asparagine-linked oligosaccharide derivatives can be immediately used, for example, for glycopeptides synthesis. (Paragraph [0033])

Specifically, claim 1 recites, *inter alia*, the steps of: "(a) treating a delipidated egg yolk with orientase to obtain a mixture of peptide-linked oligosaccharides; (b) treating the mixture of peptide-linked oligosaccharides with actinase to obtain a mixture of asparagine-linked oligosaccharides." In like manner, claim 14 requires, *inter alia*, the steps of: "(a) treating a delipidated egg yolk with a protease to obtain a mixture of peptide-linked oligosaccharides; (c) treating the isolated mixture of peptide-linked oligosaccharides with a peptidase to obtain a mixture of asparagine-linked oligosaccharides."

Koketsu 1995 teaches a one-step enzymatic process for preparing sialyglycopeptides using Orientase to treat the delipidated egg yolk. (*See* page 838, under "Experimental"). However, the resulting glycopeptides, A-I and A-II, are a mixture of glycopeptides having 1 to 3.5 amino acids. (*See* page 835, lines 9-11). NMR data show that A-II glycopeptides have the same sugar chains as those on the asparagine-linked oligosaccharide derivatives of the present invention. However, A-II glycopeptides contain two amino acid residues, i.e., Asn and Lyn. (*See* page 837, lines 6-12).

The Examiner asserts that Koketsu 1995 teaches a process for preparing asparagine-linked oligosaccharide derivatives. However, Koketsu 1995 merely teaches a method of obtaining a mixture containing at least two kinds of glycopeptides in terms of the structures of the sugar chains (A-I and A-II). Koketsu 1995 never teaches a method of obtaining the specific sugar chains linked to "asparagine" only, as required by the present claims.

Specifically, Koketsu 1995 and SCORE search result (for the asparagine-linked oligosaccharide structural formula) do not teach or suggest a second step of enzymatic process: "(b) treating the mixture of peptide-linked oligosaccharides with actinase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 1; or "(c) treating the isolated mixture of peptide-linked oligosaccharides with a peptidase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 14.

Yamamoto 1996 teaches a method for preparing sialic acid-containing oligosaccharides, but not asparagine-linked oligosaccharides. Specifically, Yamamoto 1996 teaches that conventional methods for preparing oligosaccharides by directly treating delipidated egg yolk with proteases require a large quantities of proteases. Therefore, Yamamoto 1996

teaches a method to solve this problem by first extracting the delipidated egg yolk with water or a salt solution before enzyme treatments. (*See* paragraphs [004], [0005], and [0007]). Thus, Yamamoto 1996 teaches away from directly treating the delipidated egg yolk with enzymes.

Furthermore, Yamamoto 1996 discloses sialic acid-containing oligosaccharides in the form of (i) free oligosaccharides without any amino acid, or (ii) glycopeptides (with one or more sialic acids) having one or more amino acid. (*See* paragraph [0004]). In other words, the process of Yamamoto 1996 produces a mixture of oligosaccharides with zero, one, or more amino acids. In contrast, oligosaccharides produced by methods of the present invention are linked to a single amino acid, asparagine.

Furthermore, Yamamoto 1996 also teaches that the sialic acid-containing oligosaccharides may be treated with peptide N-glycanase to release the sugar chains from the peptide. Thus, Yamamoto 1996 did not intend to obtain asparagine-linked oligosaccharide derivatives that contain only asparagine.

Therefore, a combination of Koketsu 1995 with Yamamoto 1996 would not teach or suggest every limitation of the present claims. Specifically, a combination of Koketsu 1995 with Yamamoto 1996 would not teach the step of "(b) treating the mixture of peptide-linked oligosaccharides with actinase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 1; or "(c) treating the isolated mixture of peptide-linked oligosaccharides with a peptidase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 14.

In view of the above, a skilled artisan would not be motivated to combine Koketsu 1995 with Yamamoto 1996 to come up with the present invention. As a result, Koketsu

1995 and SCORE search result in view of Yamamoto 1996 cannot render claims 1 and 14 obvious. Therefore, claims 1 and 14 are patentable over Koketsu 1995 and SCORE search result in view of Yamamoto 1996.

Inazu does not teach or suggest the step of "(b) treating the mixture of peptide-linked oligosaccharides with actinase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 1; or the step of "(c) treating the isolated mixture of peptide-linked oligosaccharides with a peptidase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 14. The Examiner relies on Inazu to teach introducing a lipophilic protective group and subjecting the mixture of asparagine-linked oligosaccharide derivatives to a fractionating chromatography.

Koketsu 1993 also does not teach or suggest the step of "(b) treating the mixture of peptide-linked oligosaccharides with actinase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 1; or the step of "(c) treating the isolated mixture of peptide-linked oligosaccharides with a peptidase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 14, as evidenced by the fact that the Examiner relies on Koketsu 1993 to teach treating with ethanol, separating using reverse-phase column, hydrolyzing, and adding sialyoligosaccharides to drugs and foods.

Similarly, Yamamoto 2001 also does not teach or suggest the step of "(b) treating the mixture of peptide-linked oligosaccharides with actinase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 1; or the step of "(c) treating the isolated mixture of peptide-linked oligosaccharides with a peptidase to obtain a mixture of asparagine-linked oligosaccharides," as required by claim 14, as evidenced by the fact that the Examiner relies on

Yamamoto 2001 to teach the motivation for introducing a lipophilic protection group and hydrolyzing the asparagine-linked oligosaccharides and the reasonable expectation of success of treating delipidated egg yolk with actinase E.

Thus, Koketsu 1995 and SCORE search result in view of Yamamoto 1996, further in view of Inazu, Koketsu 1993, and Yamamoto 2001 would not teach or suggest every limitation of claims 1 or 14. Therefore, claims 1 and 14 are patentable over Koketsu 1995 and SCORE search result in view of Yamamoto 1996, further in view of Inazu, Koketsu 1993, and Yamamoto 2001. The dependent claims should also be patentable for at least the same reasons. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

Applicant believes this reply is fully responsive to all outstanding issues and places this application in condition for allowance. If this belief is incorrect, or other issues arise, the Examiner is encouraged to contact the undersigned or his associates at the telephone number listed below. Please apply any charges not covered, or any credits, to Deposit Account 50-0591 (Reference Number 17563/004001).

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Respectfully submitted,

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